CLAIMS

1. Process for the synthesis of compounds of formula (I)

$$\begin{array}{c}
H \\
(S) \\
H \\
CO_2H
\end{array}$$

$$\begin{array}{c}
H \\
CO_2H
\end{array}$$

$$\begin{array}{c}
H \\
H_3C \\
\end{array}$$

$$\begin{array}{c}
NHR
\end{array}$$

wherein R represents a hydrogen atom or a protecting group for the amino function,

5 characterised in that the benzyl ester of formula (IIIa) or (IIIb):

or an addition salt of the ester of formula (IIIa) or (IIIb) with a mineral acid or organic acid is reacted

with the alanine compound of formula (IV):

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wherein R' represents a protecting group for the amino function,

in the presence of a coupling agent selected from the following reagents and pairs of reagents:

- (1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride,
- 15 (1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / 1-hydroxybenzotriazole,

- (1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / 1-hydroxy-7-azabenzo-triazole,
- (1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / N-hydroxysuccinimide,
- (1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / 3-hydroxy-3,4-dihydro-
- 5 4-oxo-1,2,3-benzotriazine,
 - (1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / N-hydroxyphthalimide,
 - dicyclohexylcarbodiimide / 1-hydroxy-7-azabenzotriazole,
 - dicyclohexylcarbodiimide / N-hydroxysuccinimide,
 - dicyclohexylcarbodiimide / 3-hydroxy-3,4-dihydro-4-oxo-1,2,3-benzotriazine,
- 10 dicyclohexylcarbodiimide / N-hydroxyphthalimide,
 - O-(benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate,
 - O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate,
 - O-(benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate,
 - benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate,
- benzotriazol-1-yl-oxy-tris(dimethylamino)phosphonium hexafluorophosphate,
 - O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate,
 - O-(benzotriazol-1-yl)-1,1,3,3-bis(pentamethylene)uronium hexafluorophosphate,
 - chloro-tripyrrolidinophosphonium hexafluorophosphate,
 - chloro-1,1,3,3-bis(tetramethylene)formamidinium hexafluorophosphate,
- 20 chloro-1,1,3,3-bis(pentamethylene)formamidinium hexafluorophosphate,
 - N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline,
 - O-[(ethoxycarbonyl)-cyanomethyleneamino]-1,1,3,3-tetramethyluronium tetrafluoroborate,
 - O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoro-borate,
- O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate / 1-hydroxybenzotriazole,
 - O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoro-borate / N-methylmorpholine,
 - O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoro-
- 30 borate / collidine,
 - O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-tetramethyluronium tetrafluoroborate,

O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-tetramethyluronium tetrafluoroborate / 1-hydroxybenzotriazole,

O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate,

O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-bis(tetramethylene)uronium hexafluoro-

5 phosphate / 1-hydroxy-benzotriazole,

O-(N-succinimidyl)-1,1,3,3-tetramethyluronium tetrafluoroborate,

O-(N-succinimidyl)-1,1,3,3-bis(tetramethylene)uronium tetrafluoroborate,

O-(N-succinimidyl)-1,1,3,3-bis(tetramethylene)uronium tetrafluoroborate / 1-hydroxy-benzotriazole,

O-(5-norbornene-2,3-dicarboximido)-1,1,3,3-tetramethyluronium tetrafluoroborate, propanephosphonic anhydride,

N-hydroxy-5-norbornene-2,3-dicarboxylic acid imide, and N-hydroxy-1,2-dihydro-2-oxo-pyridine,

optionally in the presence of a base,

to yield the compound of formula (Va) or (Vb), respectively, depending on whether the compound of formula (IIIa) or (IIIb) is used as starting material:

$$H_{3}C_{(S)}$$

$$NHR'$$

$$(Va)$$

$$(S)$$

$$N CO_{2}Bn$$

$$H_{3}C_{(S)}$$

$$NHR'$$

$$(Vb),$$

wherein R' is as defined hereinbefore,

which is subjected to a catalytic hydrogenation reaction in the presence of palladium to yield the product of formula (I).

2. Process according to claim 1, characterised in that the compound of formula (IIIa) is used as starting material.

- 3. Process according to claim 1, characterised in that the compound of formula (IIIb) is used as starting material.
- 4. Process according to claim 2, characterised in that the hydrogenation reaction on the compound of formula (Va) is carried out under a hydrogen pressure of less than 10 bars.

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- 5. Process according to claim 3, characterised in that the hydrogenation reaction on the compound of formula (Vb) is carried out under a hydrogen pressure of from 10 to 35 bars.
- 6. Process for the synthesis of perindopril or pharmaceutically acceptable salts thereof starting from a compound of formula (I), characterised in that the said compound of formula (I) is obtained by the synthesis process according to any one of claims 1 to 5.